can be found in the originally filed claims as well as throughout the specification. No new matter is added to the specification by these changes.

I. Rejection under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 50-55, 60, 63-66, 79-81, 84-91, 94-97, 102-104, 108-109, 111-112, 122-123, 125-126, 129, 136-150, and 153-156 stand rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant has replaced the term "allergic antigen" with "allergen" in the newly drafted claims; therefore, Applicant submits that the rejection is obviated by the Amendment submitted herewith.

II. Rejection under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps. Claims 50-55, 60, 63-66, 79-81, 84-91, 94-97, 102-104, 108-112, 115-116, 122-123, 125-126, 129, 136-139, 142-150, 153-156, 160-175, 184-185, and 188-191 stand rejected under 35 USC § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. Applicant *strongly* disagrees with the Examiner's position that essential steps have been omitted. The specification *defines* immune system response to include events that occur *in vivo* or *in vitro*. The Examiner does not like this definition because "the disclosure on page 24, line 5 is not sufficient to overcome the art-recognized definitions". Applicant respectfully submits that a disclosure provides its own definition, which definition is binding unless it is repugnant to an art-recognized definition. In this case, the art-recognized definition, according to the Examiner, is that an "immune system" or an "immune response" "encompasses an *in vivo* response". Applicant does not disagree that the art-recognized definition encompasses an *in vivo* response. It is Applicant's position, however, that the art-recognized definition *is not limited to* an *in vivo* response. Moreover, even if it were, the present specification makes abundantly clear that the terms "immune response" and "immune system" are not limited to *in vivo* responses or systems for the purposes of the present invention.

In this regard, Applicant points out that an entire section of the disclosure is directed to

modulating immune responses *in vitro* (pg 23, line 18- pg. 29, line 3). Moreover, throughout the application it is clear that an "immune system" may be an *in vivo* system or an *in vitro* system (see, for example, pg. 29, lines 6-7: "As described above, various of the inventive approaches involve delivery of one or more compounds *in vivo* or *in vitro* to a *reacting system*"; emphasis added).

Nonetheless, for the sole purpose of obviating the Examiner's rejection in the present case, Applicant has now presented claims that include a step of administration to an individual. Appplicant expressly reserves the right to pursue claims lacking this step in another filing.

III. Rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement. Claims 50-55, 60, 63-66, 79-81, 84-91, 94-97, 102-104, 108-112, 122-123, 125-126, 129, 136-139, 142-150, 153-156, 160-164, 169, 171-175, 184-185, and 188-191 stand rejected under 35 USC § 112, first paragraph, for lack of enablement. Applicant strongly disagrees with the Examiner's assertions regarding enablement, including for example that a CpG oligonucleotide is required to bias a dendritic cell response away from a Th2 response. Nonetheless, Applicant submits that these assertions are not applicable to the present claims, and the rejection for lack of enablement is therefore moot and can be removed.

IV. Rejection under 35 U.S.C. § 102(e), as being anticipated by U.S. Patent 5,994,126. Claims 50-55, 60, 109, 111-112, and 126 stand rejected under 35 U.S.C. § 102(e), as being anticipated by U.S. Patent 5,994,126. Examiner contends that the '126 patent teaches a method of modulating an immune response to an antigen comprising isolating pAPC from an individual and exposing said pAPC to a crude antigen followed by administering said pAPC to a subject.

Applicant respectfully disagrees. The '126 patent teaches a method of producing *in vitro* mature dendritic cells from proliferating cell cultures. The '126 patent does not teach exposing the pAPC to allergen *and* a factor such as CpG-containing oligonucleotides *so that an immune response to the allergen is modulated away from a Th2 response.* The entire '126 patent disclosure cited by the Examiner as relating to exposure of dendritic cells to antigen is the sentence "Amptjer embodiment of the invention are antigen-activated dendtricitc cells prepared

according to the method of the invention in which antigen-activated dendritic cells have been exposed to antigen and express modified antigens for presentation to and activation of T cells" (column 6, lines 1-5). Earlier in the Office Action, Examiner asserts "that allergens exposed to and presented by dendritic cells *drive IgE production in Th2 cell-driven responses* . . . Therefore, in the absence of . . . (an inducing agent factor), the response would be driven *toward* a Th2 response rather than away from a Th2 response" (page 7; emphasis in original). By the Examiner's own argument, the '126 patent *cannot* anticipate the presently claimed invention. Nor could the '126 patent render obvious the present claims; in fact, it strongly teaches away from the presently claimed invention. The rejection for lack of novelty over the '126 patent should be removed.

V. **Rejection under 35 U.S.C. §103(a)**. Claims 50-55, 60, 63-66, 79-81, 84-91, 94-97, 102-104, 108-112, 122-123, 125-126, 129, 136-139, 142-150, 153-156, 160-164, 169, 171-175, 184-185, and 188-191 stand rejected under 35 USC §103(a) as being unpatentable over U.S. Patent 5,994,126 in view of WO98/37919, WO98/33520, and others. As noted above, the '126 patent *cannot* teach or suggest the claimed invention, and in fact teaches away from methods is which APCs are exposed to allergen under conditions selected such that a subsequent immune response to the allergen is biased *away from* a Th2 response. None of the other cited references can correct this deficiency. The Examiner has selected references that disclose an individual encapsulating device, targeting agent, type of antigen preparation, or inducing agent factor that could be used in the practice of the present invention. However, none of the references, alone or in combination, teach or suggest the claimed methods. For example, even if, as asserted by the Examiner, Maurer et al. teach that FcR ligands can facilitate the uptake of antigen by a dendritic cell, combining this disclosure with the '126 patent cannot render obvious the claimed invention. Maurer et al. provide no teaching or suggestion of modulating an immune response away from a Th2 response. The extent of the disclosure in Maurer et al. relating to the effect of their facillitated allergen uptake is that "FceRI/IgE-dependent allergent uptake by DC may both quantitatively and qualitatively modulate allergen presentation *in vitro* and may have profound implications on the magnitude and diversification of allergen-specific T cell responses in human

disease" (pg. 177). According to the Examiner's own arguments, effects on allergen presentation *in vitro* are not modulation of immune responses as recited in the present claims. Furthermore, "profound implications on the magnitude and diversification of allergen-specific T cell responses in human disease" gives no indication of the desirability, let alone likely success of modulating a response away from a Th2 response.

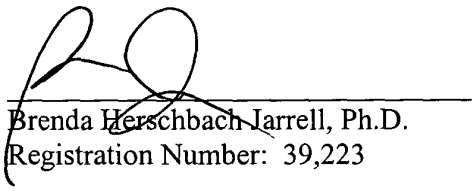
The Examiner cites relies heavily on WO 98/37919 for providing motivation to bias an immune response away from a Th2 response. Even if the Examiner is correct that the '919 application provides such a general motivation, it provides no motivation, let alone any guidance or likelihood of success, for exposing isolated dendritic cells to allergen under conditions that affect the dendritic cells so that subsequent immune responses to allergen are biased away from Th2 reactions. WO 98/37919 teaches the administration of CpG-containing oligonucleotides to a subject to redirect the subject's immune response *in vivo*. WO 98/37919 does not teach the contacting of a factor such as a CpG-containing oligonucleotide with cells *in vitro*, and it certainly does not teach contacting dendritic cells with a factor *in vitro*.

As noted above, the '126 patent provides no teaching or suggestion of the desirability or feasibility of modulating dendritic cells in this way; the Examiner is therefore relying on hindsight reconstruction. Having read the present application and considered the present claims, the Examiner now recognizes the desirability and feasibility of exposing isolated APC to allergen under conditions that result in a bias, in a subsequent immune response, away from Th2. With the benefit of this insight, the Examiner has now looked back at the art and attempted to reconstruct pieces of the invention; such hindsight reconstruction is impermissible and cannot be used to invalidate the present claims. The Examiner's conclusory statements that both motivation to try and reasonable expectation of success can be found in the prior art are not legally sufficient to support an obviousness rejection; the rejection should be removed.

In view of the forgoing arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,



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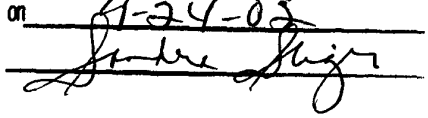

Appendix A

Claims Pending After Entrance of the Present Amendment

282. A method of modulating an immune system response to an allergen, the method comprising steps of:

isolating from an individual one or more professional antigen presenting cells (pAPC);

exposing the isolated cells to an allergen and a factor selected from the group consisting of LPS, CD40, CD40 ligand, BCGs, oligonucleotides containing CpG motifs, TNF-α, microbial extracts, IL-12, IL-2, IL-18, IL-1β, fragments of IL-1β, IFNα, and IFNγ; and

administering the allergen-exposed pAPC to the individual so that immune response of the individual to the allergen is modulated away from a Th2 response.

283. The method of claim 282, wherein the professional antigen presenting cells are selected from the group consisting of mature pAPC, immature pAPC, and precursors to pAPC.

284. The method of claim 282, wherein the pAPC are mature pAPC.

285. The method of claim 282, wherein the pAPC are immature pAPC.

286. The method of claim 282, wherein the pAPC are selected from the group consisting of dendritic cells, B-cells, and macrophages.

287. The method of claim 282, wherein the pAPC are dendritic cells.

288. The method of claim 282, wherein the step of exposing comprises exposing the cells to a crude allergen preparation.

289. The method of claim 282, wherein the step of exposing comprises exposing the cells to a

substantially pure allergen.

290. The method of claim 282, wherein the step of exposing comprises contacting the cells with an allergen that is associated with a targeting agent.

291. The method of claim 282, wherein the microbial extracts are selected from the group consisting of any *Staphylococcus aureus* preparation, heat-killed *Listeria*, and modified cholera toxin.

292. The method of claim 282, wherein one or both of the allergen and factor are associated with a targeting agent.

293. The method of claim 292, wherein the targeting agent is selected from the group consisting of a mannose receptor ligand, a Fc receptor ligand, a complement receptor ligand, and DEC205.

294. The method of claim 292, wherein the targeting agent is capable of targeting to intracellular vesicles within pAPCs.

295. The method of claim 292, wherein the targeting agent comprises at least the Fc portion of an Ig molecule.

296. The method of claim 292, wherein the targeting agent comprises at least the Fc portion of an IgG molecule.

297. The method of claim 282, wherein one or both of the allergen and factor are encapsulated.

298. The method of claim 282, wherein the allergen and factor are encapsulated together.

299. The method of claim 282, wherein the allergen and factor are encapsulated separately.

300. The method of claim 296, wherein one or both of the allergen and factor are encapsulated and associated with a targeting agent.

301. The method of claim 282 wherein the step of exposing comprises exposing the cells to a modified allergen.

302. The method of claim 282 further comprising administering allergen to the individual.

303. A method of modulating an immune system response to an allergen, the method comprising steps of:

isolating from an individual one or more professional antigen presenting cells (pAPC);

exposing the isolated cells to an allergen and a factor selected from the group consisting of LPS, CD40, CD40 ligand, BCGs, oligonucleotides containing CpG motifs, TNF-α, microbial extracts, IL-12, IL-2, IL-18, IL-1β, fragments of IL-1β, IFNα, and IFNγ;

contacting the antigen-exposed pAPC with T-cells so that a Th2 response is inhibited; and

administering the T-cells to the individual so that immune response of the individual to the allergen is modulated away from a Th2 response.

304. The method of claim 303, wherein the professional antigen presenting cells are selected from the group consisting of mature pAPC, immature pAPC, and precursors to pAPC.

305. The method of claim 303, wherein the step of contacting comprises contacting the antigen-exposed pAPC with T-cells in the presence of a Th1 inducing agent selected from the group consisting of LPS, CD40, CD40 ligand, BCGs, oligonucleotides containing CpG motifs,

THFα, microbial extracts, IL-12, IL-2, IL-18, IL-1β, fragments of IL-1β, IFNα, and IFNγ.

306. The method of claim 305, wherein the microbial extracts are selected from the group consisting of any *Staphylococcus aureus* preparation, heat-killed *Listeria*, and modified cholera toxin.

307. The method of claim 303, wherein the pAPC are selected from the group consisting of dendritic cells, B cells, and macrophages.

308. The method of claim 303, wherein the pAPC are dendritic cells.

309. The method of claim 303, wherein the step of contacting is performed concurrently with the step of exposing to allergen and factor.

310. The method of claim 303, wherein the step of exposing comprises exposing the cells to a crude allergen preparation.

311. The method of claim 303, wherein the step of exposing comprises exposing the cells to a substantially pure allergen.

312. The method of claim 303, wherein the step of exposing comprises exposing the cells to an allergen that is associated with a targeting agent.

313. The method of claim 303, wherein one or both of the allergen and factor are associated with a targeting agent.

314. The method of claim 312, wherein the targeting agent is selected from the group consisting of a mannose receptor ligand, a Fc receptor ligand, a complement receptor ligand, and DEC205.

315. The method of claim 312, wherein the targeting agent is capable of targeting to intracellular vesicles within pAPCs.

316. The method of claim 312, wherein the targeting agent comprises at least the Fc portion of an Ig molecule.

317. The method of claim 312, wherein the targeting agent comprises at least the Fc portion of an IgG molecule.

318. The method of claim 303, wherein one or both of the allergen and factor are encapsulated.

319. The method of claim 303, wherein the allergen and factor are encapsulated together.

320. The method of claim 303, wherein the allergen and factor are encapsulated separately.

321. The method of claim 303, wherein one or both of the allergen and factor are encapsulated and associated with a targeting agent.

322. The method of claim 303, wherein the step of exposing comprises exposing the cells to a modified allergen.

323. A method of treating allergy, the method comprising steps of:

identifying an individual who is allergic to an allergen;

providing a composition of professional antigen presenting cells (pAPC) displaying the allergen;

contacting the composition with T-cells of the individual in the presence of a factor selected from the group consisting of LPS, CD40, CD40 ligand, BCGs, oligonucleotides

containing CpG motifs, TNF-α, microbial extracts, IL-12, IL-2, IL-18, IL-1β, fragments of IL-1β, IFNα, and IFNγ; and

administering the T-cells to the individual so that immune response of the individual to the allergen is modulated away from a Th2 response.

324. The method of claim 323, wherein the professional antigen presenting cells (pAPC) are selected from the group consisting of mature pAPC, immature pAPC, and precursors of pAPC.

325. The method of claim 323, wherein the microbial extracts are selected from the group consisting of any *Staphylococcus aureus* preparation, heat-killed *Listeria*, and modified cholera toxin.

326. The method of claim 323, wherein the pAPC are selected from the group consisting of dendritic cells, B cells, and macrophages.

327. The method of claim 323, wherein the pAPC are dendritic cells.

328. The method of claim 323, wherein the step of providing comprises:

isolating from the individual one or more professional antigen presenting cells (pAPC); and

exposing the isolated cells to the allergen and a factor selected from the group consisting of LPS, CD40, CD40 ligand, BCGs, oligonucleotides containing CpG motifs, TNF-α, microbial extracts, IL-12, IL-2, IL-18, IL-1β, fragments of IL-1β, IFNα, and IFNγ.

329. The method of claim 328, wherein the microbial extracts are selected from the group consisting of any *Staphylococcus aureus* preparation, heat-killed *Listeria*, and modified cholera toxin.

330. The method of claim 328, wherein one or both of the allergen and factor are associated

with a targeting agent.

331. The method of claim 330, wherein the targeting agent is selected from the group consisting of a mannose receptor ligand, a Fc receptor ligand, a complement receptor ligand, and DEC205.

332. The method of claim 330, wherein the targeting agent comprises at least the Fc portion of an Ig molecule.

333. The method of claim 330, wherein the targeting agent comprises at least the Fc portion of an IgG molecule.

334. The method of claim 328, wherein one or both of the allergen and factor are encapsulated.

335. The method of claim 328, wherein the allergen and factor are encapsulated together.

336. The method of claim 328, wherein the allergen and factor are encapsulated separately.

337. The method of claim 328, wherein one or both of the allergen and factor are encapsulated and associated with a targeting agent.